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EXAMINER	
WANG, CHANG YU	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/669,853	SAH, DINAH W. Y.	
	Examiner	Art Unit	
	Chang-Yu Wang	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 July 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,5,10-12,35-37,57-65 and 67-81* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,5,10-12,35-37,57-65 and 67-81* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/27/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

RESPONSE TO AMENDMENT

Status of Application/Amendments/claims

1. Applicant's amendment filed July 6, 2007 is acknowledged. Claims 2-3, 6-9, 13-34, 38-56, 66 are cancelled. Claims 1, 4-5, 10-12, 35-37, 57-65, 67-70 and newly added claims 71-81 are pending and under examination in this office action.

2. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response.

3. Applicant's arguments filed on July 6, 2007 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Information Disclosure Statement

4. The information disclosure statement filed November 27, 2006 fails to comply with 37 CFR 1.98(a)(1), which requires the following: (1) a list of all patents, publications, applications, or other information submitted for consideration by the Office; (2) U.S. patents and U.S. patent application publications listed in a section separately from citations of other documents; (3) the application number of the application in which the information disclosure statement is being submitted on each page of the list; (4) a column that provides a blank space next to each document to be considered, for the examiner's initials; and (5) a heading that clearly indicates that the list is an information disclosure statement, such as a form of PTO-1449. The information disclosure

statement has been placed in the application file, but the information referred to therein has not been considered.

Applicant submitted an IDS on Nov 27, 2006 and requested consideration of an attached communication from a foreign patent office. However, no such copy of the communication was provided in the IDS submitted on 11/27/06. In addition, the IDS submitted by this manner is not an appropriate format.

Claim Rejections/Objections Withdrawn

5. The objection to claim 2 is moot because the claim is canceled.

Claim Rejections/Objections Maintained

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4-5, 10-12, 35-37, 57-65, 67-70 and 71-81 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of improving the behavior tests on a mouse model of tactile allodynia and thermal hyperalgesia (Chung L5/L6 spinal nerve ligation (SNL) model) and a mouse model of diabetic neuropathy induced by streptozotocin (STZ) by administering SEQ ID NO:2 or a polypeptide consisting of aa 28-140 of SEQ ID NO:2 (NBN113) to the test mice, does not reasonably provide enablement for a method of treating neuropathic

pain associated with diabetic neuropathy in a subject using neublastin polypeptides with limited homology as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. The rejection is maintained for the reasons made of record in the office action mailed 1/9/07 and as follows.

At p. 8-9 of the response, Applicant argues that a person of skill in the art would know how to make neublastin polypeptides with at least 85% identity to aa 28-140 of SEQ ID NO:2 to maintain neublastin biological activity because the specification provides standard mutagenesis methods and screening assays as disclosed in WO00/01815, and the truncated forms of neublastin (aa 42-140 and aa 37-140 of SEQ ID NO:2) having neurotrophic activity have been disclosed in US2002/0055467 and US2004/0142418. Applicant's arguments have been fully considered but they are not persuasive.

In contrast to Applicants' assertion, the standard of enablement is not just how to make and test, but whether the skilled artisan would reasonably know what critical amino acid residues are required for guiding one of ordinary skill in the art to make a functional polypeptide with a reasonable expectation of success; consistent with that held by the court in *In re Wands*. In contrast, Applicant discloses a single functional polypeptide (i.e. aa 28-140 of SEQ ID NO:2 or SEQ ID NO:2), in which no correlation between structure and function is disclosed for their "variant" polypeptides. As previously made of record, the specification fails to define what specific amino acids are

critical for the function of SEQ ID NO:2 or aa 28-140 of SEQ ID NO:2 or aa 37-140, or aa 42-140 of SEQ ID NO:2, nor what amino acid residues distinguish the instant invention from any different variant SEQ ID NO:2 or aa 28-140 of SEQ ID NO:2-related proteins with different functional activities. Accordingly, the skilled artisan would not reasonably expect that random mutations manifested within a variant aa 28-140 of SEQ ID NO:2 or aa 37-140 or aa. 42-140 of SEQ ID NO:2 polypeptide would result in an active polypeptide.

Although many amino acid substitutions are possible in any given protein, as previously made of record, the position of where such amino acid substitutions can be made is critical for maintaining the function of a protein; i.e. only certain positions can tolerate conservative substitutions without changing the relationship of three dimensional structure and function of the protein. Although the specification outlines art-recognized procedures for producing and the screening method, this is not adequate guidance as to the nature of active neublastin polypeptides that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation.

At p. 10 of the response, Applicant further argues that no undue experimentation is required to identify variants of neublastin polypeptides that retain neublastin biological activity because In *In re Wands*, the court did not find screening many hybridomas to find the few within the claims as undue experimentation in support of the argument. Applicant's arguments have been fully considered but they are not persuasive.

In contrast, because of the lack of guidance provided in the specification as to what minimal structural requirements are necessary for any "variants" with at least 85% identity to aa 28-140 of SEQ ID NO:2 that result in treating neuropathic pain associated with diabetic neuropathic pain, the skilled artisan would not reasonably know how to make and use the instant invention, as currently claimed, without requiring undue experimentation to determine otherwise, and for the reasons previously made or record. Accordingly, the court in *Genentech, Inc., v. Novo Nordisk*, 42 USPQ2d 1001, 1005 (1997), held that

> "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable", and that "reasonable detail must be provided in order to enable members of the public to understand and carry out the invention".

In that limited structure and little functional language (i.e., "neurotrophic activity") is recited in the claims, the claims encompass using any variant polypeptide, which are unpredictable whether they have the same activity as aa 28-140 of SEQ ID NO:2 or SEQ ID NO:2 in treatment of neuropathic pain associated with diabetic neuropathy. Thus, the rejection of claims 1, 4-5, 10-12, 35-37, 57-65, 67-70 and 71-81 under 35 U.S.C. §112, first paragraph, because the specification does not enable the invention commensurate in scope with the claims is maintained.

7. Claims 1, 4-5, 10-12, 35-37, 57-65, 67-81 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the

application was filed, had possession of the claimed invention. The rejection is maintained for the reasons made of record in the office action mailed on 1/9/07, and as follows.

At p.11-12 of the response, Applicant argues that independent claim 1 is directed to use of a structurally and functionally defined polypeptide because the claimed genus of variant neublastin polypeptides having at least 85% identity to aa 28-140 of SEQ ID NO:2 have neurotrophic activity, and the activity of truncated forms of neublastin polypeptides are also disclosed in US2002/0055467 and US20040142418. Applicant's arguments have been fully considered but they are not persuasive.

In contrast to Applicant's assertion that amended claims are directed to use of structurally and functionally defined polypeptides in treatment of neuropathic pain, the examiner asserts that the claimed genus of variant neublastin polypeptides having at least 85% identity to aa 28-140 of SEQ ID NO:2 or at least 85% identity to aa 37-140 or 42-140 of SEQ ID NO:2 are not structurally and functionally defined because the specification fails to provide sufficient description as to what specific amino acid sequences are required and need to be conserved in order to preserve the function of aa 28-140 of SEQ ID NO:2 or SEQ ID NO:2. The specification does not reasonably demonstrate Applicant's possession of such claimed genus of neublastin polypeptides to be used in the claimed method of treating neuropathic pain.

In this case, only aa 28-140 of SEQ ID NO:2 and SEQ ID NO:2 have been described in the instant specification to be used in the claimed method for treating neuropathic pain associated with diabetic neuropathy. However, the claims are not

limited to the molecules as set forth above but also encompassed variants of aa 28-140, aa 37-140 and aa 42-140 of SEQ ID NO:2.

As previously made of record, *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111, 1117, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, *as of the filing date sought*, he or she was in possession *of the claimed invention*". The court held in *Univ. California v. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997) that:

"One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is".

and that:

"A description of a genus of cDNAs [products] may be achieved by means of a recitation of a representative number of cDNAs [products], *defined by nucleotide sequence*, failing in the scope of the genus or of a recitation of structural features common to the members of the genus, *which features constitute a substantial portion of the genus* [emphasis added]. This is analogous to enablement of a genus under 112, [first paragraph], by showing the enablement of a representative number of species within the genus. See *In re* Angstadt, 537 F.2d at 502-03, 190 USPQ at 218".

In contrast, as previously made of record, the instant specification fails to provide sufficient description to demonstrate Applicant's possession of the claimed genus of neublastin polypeptides to be used in the claimed method because what particular portions of the structure must be conserved, with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics for the claimed genus of neublastin polypeptides has not reasonably been provided within the instant specification. In addition, the instant specification provides an invitation for others to discover a representative number of species (i.e. variants of

neublastin polypeptides with at least 85% identity to aa 28-140 of SEQ ID NO:2) that can be used in the claimed method of treating neuropathic pain associated with diabetic neuropathy. Furthermore, although aa 37-140 or 42-140 of SEQ ID NO:2 has neurotrophic activity as disclosed in copending applications, the claims are not limited aa 37-140 and 42-140 of SEQ ID NO:2 but also include variants of aa 37-140 and aa 42-140 of SEQ ID NO:2. Applicant fails to provide what specific amino acid sequences and common structures and features are required for the claimed variants to be used in treatment of neuropathic pain. Thus, Applicant was not reasonably in possession of the "claimed genus of neublastin polypeptides" that can be used in the claimed method, and for the reasons previously made of record. See again MPEP 2163. Therefore, the rejection of claims 1, 4-5, 10-12, 35-37, 57-65, 67-81 under 35 U.S.C.§ 112, first paragraph, for failing to meet the written description is maintained.

Obviousness-Type Non-Statutory Double Patenting

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to

be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 4-5, 10-12, 35-37, 57-65, 67-81 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 28 and 34 of copending Application No. 10/356264 (US20050142098) ('264) and claims 15-24 of copending Application No. 10/553710. The rejection is maintained for the reasons made of record in the office action mailed on 1/9/07, and as follows.

At p. 13 of the response, Applicant argues that copending application Nos.10/536264 and 10/553710 have not been patented and if the rejection is the only rejection remaining in the present application, the ODP should be withdrawn to allow the instant to issue as a patent and no terminal disclaimer is required. Applicant's arguments have been fully considered but they are not persuasive.

In response, based on MPEP, the condition of withdrawing a double patenting rejection and addressing the issue of double patenting in the later-filling application is under no other rejection remaining in at least one of the applications except double patenting rejection in the office action.

The "provisional" double patenting rejection should continue to be made by the examiner in each application as long as there are conflicting claims in more than one application unless that "provisional" double patenting rejection is the only rejection remaining in at least one of the applications. See MPEP § 804 [R5]-I.

Currently, no subject matter is allowable and there are other rejections in this office action. The rejection of claims under obviousness double patenting for being unpatentable over claims 28 and 34 of copending Application No. 10/356264 and claims

15-24 of copending Application No. 10/553710 is maintained until a terminal disclaimer is filed. It is noted that traversal at the time of indication of allowable subject matter will not be considered timely.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 4-5, 10, 35-37, 57-65, 67-81 are rejected under 35 U.S.C. 102 (e) as being anticipated by U.S. Patent No. 6734284 (issued on May 11, 2004, priority date Jul 9, 1998, as cited in IDS). The rejection is maintained for the reasons made of record in the office action mailed on 1/09/07, and as follows.

At p. 13 of the response, Applicant argues that neublastin was the first growth factor found to be able to reverse experimental neuropathic pain following systemic administration as published in Gardell et al. (Nat Med 2003. 9: 1383-89, as in IDS), which is an academic publication of the claimed invention. Applicant's arguments have been fully considered but they are not persuasive.

In contrast to Applicant's assertion, as previously made of record, US'284 has disclosed a method of treatment of neuropathic pain associated with diabetic pain by

administration of a neublastin polypeptide prior to the claimed invention. A description that neublastin is the first growth factor to reverse experimental neuropathic pain in an academic publication does not render the claimed invention patentable over the prior art because the claimed method using a neublastin polypeptide to treat neuropathic pain has been disclosed in US'284. US'284 discloses the claimed method of treatment of neuropathic pain using a neublastin polypeptide, which anticipates the instantly claimed method. A prior art of an issued US patent is a reference containing an "enabling disclosure" that the public was in possession of the claimed invention before the date of invention. In *In re Donhue*, the court held that

"Such possession is effected if one of ordinary skill in the art could have combined the publication's description of the invention with his [or her] own knowledge to make the claimed invention." *In re Donohue*, 766 F.2d 531, 226 USPQ 619 (Fed. Cir. 1985). See MPEP 2121.01

Thus, the claimed method of the instant application is unpatentable over the prior art US'284.

At p. 14 of the response, Applicant argues that US'284 does not anticipate the claimed method because it only provides a working example of administration of neublastin polypeptide to a model of Parkinson's disease but no a working example for treating neuropathic pain. Applicant's arguments have been fully considered but they are not persuasive.

In response, based on MPEP, an actual working example is not required for compliance with the enablement requirement of 35 U.S.C. 112, first paragraph.

"An example may be 'working' or 'prophetic.' A working example is based on work actually performed. A prophetic example describes an embodiment of the invention based on predicted results rather than work actually conducted or results actually achieved."

and also In *in re Borkowski*, the court held that

"The specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation. *In re Borkowski*, 422 F.2d 904, 908, 164 USPQ 642, 645 (CCPA 1970). See MPEP § 2164.02.

In this case, US'284 teaches using the neublastin polypeptide to treat several neuropathies including injury/trauma-induced neuropathies, chemotherapy-induced neuropathies such as neuropathies induced by delivery of Taxol, drug-induced neuropathies, and diabetic neuropathies (i.e. as in claims 1, 4, 5, 57-65, 67-81; see col. 21 lines 30-57) and are incorporated by references as disclosed in US Patent Nos. 5496804 and 5916555. As previously made of record, the neuropathic pain, allodynia, hyperalgesic pain, tactile allodynia and thermal hyperalgesic pain (i.e. claims 35-37 and 57) are derived from and are accompanied with several pathological conditions including neuropathies as mentioned above, which are evidenced by Campbell et al. (see p. 78, 1st col., 2nd paragraph to 2nd col. 2nd paragraph, Neuron. 2006. 52: 77-92 as cited in the previous action). US'284 also teaches several delivery routes including intravenous, intraperitoneal and subcutaneous administration (i.e. as in claims 58-65; see col. 18, lines 45-67), which result in systemic delivery (i.e. as in claim 1). US'284 also teaches different ways to formulate the polypeptide for specific administration routes and time-release (i.e. as in claim 10; see col.19, lines 33-42).

At p. 14 and p. 16 of the response, Applicant argues that US'284 does not teach the claimed method because US'284 does not teach systemic delivery of a neublastin polypeptide to a subject suffering from neuropathic pain associated with diabetic neuropathy and US'284 only describes different administrative routes including

intravenous, intramuscular, intrathecal, intraperitoneal, subcutaneous and inhalation etc. In contrast, as previously made of record, US'284 does teach administration routes including systemic delivery to treat neuropathic pain associated with diabetic neuropathy because US'284 teaches delivery routes including intravenous, intraperitoneal and subcutaneous administration (i.e. as in claims 58-65; see col. 18, lines 45-67), which result in systemic delivery (i.e. as in claim 1).

10. Claims 1, 4-5, 10-12, 35-37, 57-65, 67-81 are rejected under 35 U.S.C. 102(e) as being anticipated by copending Application No. 10/356264 (US20050142098). The rejection is maintained for the reasons made of record in the office action mailed on 1/9/07, and as follows.

At p. 17 of the response, Applicant argues that the rejection should be withdrawn because Applicant's declaration shows that the subject mater of the instant application is solely invented by the Applicant.

In contrast, the declaration under 37 CFR 1.132 filed 7/6/07 is insufficient to overcome the rejection of claims 1-17 based upon specific references under 35USC 102 (e) for the reasons made of record in the office action mailed on 1/9/07, and as follows.

Based on MPEP § 706.02 (f) (2) and § 715.01 (a), the rejection under 35 USC 102 (e) can be overcome by showing any invention disclosed but not claimed in the reference was derived from the inventor of this application. However, the instant claimed invention is also claimed in 10/356264 (US20050142098), which is rejected

under ODP (see paragraph 8 and the previous office action). Thus, the rejection under 35USC 102 (e) cannot be overcome by the instant declaration because the claimed subject matter in the instant application is also claimed in the copending application 10/356264. Accordingly, the statement that "the subject mater of claims.. of the '853 application was invented solely by me" and the statement "To the extent that US provisional application no. 60/266, 071 disclosed but does not claim the subject matter of any of these claims" at p. 1 bridging to p. 2 of the declaration are incorrect. Applicant also did not use the right language with regard to the statement "...the subject mater... of the '853 was solely by me" and the statement " 60/266071 disclosed and but does not claimed the subject mater...". The statement should be directed to that "...the claimed subject mater was disclosed and not claimed in the copending application (the reference) is derived by the Applicant" (not the instant application or provisional application). Thus, Applicant's declaration under 37 CFR 1.132 is not effective to overcome the rejection of 102 (e) that is anticipated by 10/356264 (US20050142098).

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 4-5, 10-12, 35-37, 57-65, 67-81 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6734284 in view of US Patent No. 5414135 (issued May 9, 1995, effective filing date Dec 30, 1991). The rejection is maintained for the reasons made of record in the office action mailed on 1/9/07, and as follows.

At p. 18 of the response, Applicant argues that US'284 does not anticipate the claimed method for treating neuropathic pain associated with diabetic neuropathy by administering a neublastin polypeptide via systemic delivery and US'135 does not supplement the deficiencies of '284 or to render the claimed method obvious. Applicant's arguments have been fully considered but they are not persuasive.

In contrast to Applicant's assertion, US'284 does teach the claimed method of treating neuropathic pain by systemic administration of a neublastin polypeptide to a patient suffering from neuropathic pain associated with diabetic neuropathy for the reasons set forth in the previous office action and above at paragraph 9. Although US'284 does not teach modification of neublastin polypeptides with PEG or aliphatic ester (i.e. as in claims 11 and 12), as previously made of record, US'135 teaches coupling polyethylene glycol (PEG) to proteins as in claims 10-11 to maintain

physiologically active and non-immunogenic activity of the proteins because polyethylene glycol can protect the polypeptide from loss of activity without inducing substantial immunogenic response (see col. 2, lines 30-62). In addition, US'135 also teaches modification of proteins by imino esters, which is one of aliphatic esters as recited in claim 12 (see col. 2, lines 62-68 and col. 16, example 13). Thus, it would have been obvious to one of ordinary skill in the art at the time the instant invention was made to modify neublastin polypeptides with polyethylene glycol or aliphatic esters. The person of ordinary skill in the art would have been motivated to do so to maintain activity and avoid immunogenicity of neublastin polypeptides in the claimed method of treating neuropathic pain associated with diabetic neuropathy because polyethylene glycol and aliphatic esters have been used to modify polypeptides to extend the time of protein activity and to maintain active concentration of proteins in the body.

Conclusion

12. NO CLAIM IS ALLOWED.

13. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers relating to this application may be submitted to Technology Center 1600, Group 1649 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chang-Yu Wang whose telephone number is (571) 272-4521. The examiner can normally be reached on Monday-Thursday and every other Friday from 8:30 AM to 5:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached at (571) 272-0841.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/CYW/
Chang-Yu Wang, Ph.D.
September 4, 2007

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